

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#14

In re Application of:

KOVALIC *et al.*

Appln. No.: 09/684,016

Filed: October 10, 2000

For: Annotated Plant Genes

Art Unit: 1631

Examiner: S. Zhou

Atty. Docket: 16517.031

Response to Notice of Non-Responsive CommunicationCommissioner for Patents
Washington, DC 20231

Sir:

In response to the notice of non-responsive communication mailed October 21, 2002, which alleged that Applicants failed to provide a marked-up version of claim 14, Applicants submit herewith a photocopy of the Response to the Office Action Dated May 8, 2002, which was filed on August 8, 2002, and its accompanying transmittal letter. A marked-up version of the amendments to claim 14 appears on page 17 of the Response.

In view of the foregoing remarks, it is respectfully submitted that the present application is in condition for allowance, and notice of such is respectfully requested. The Examiner is encouraged to contact the undersigned should any additional information be necessary for allowance.

In the event that extensions of time beyond those petitioned for herewith are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Applicants do not believe that any fees in addition to those provided for in the

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accompanying documents, are due at this time. However, if any fees under 37 C.F.R. 1.16 or 1.17 are required in the present application, including any fees for extensions of time, then the Commissioner is hereby authorized to charge such fees to Deposit Account No. 50-2387, referencing docket number 16517.031.

Respectfully submitted,



David R. Marsh (Reg. No. 41,408)
June E. Cohan (Reg. No. 43,741)
Danielle M. Edwards, Law Clerk (Reg. No. 51,645)

Date: November 8, 2002

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August 8, 2002

Commissioner for Patents
Washington, DC 20231

Re: U.S. Utility Patent Application No. 09/684,016
Filed: October 10, 2000
Inventor: David K. KOVALIC *et al.*
For: *Annotated Plant Genes*
Dkt. No.: 16517.031

Sir:

Transmitted herewith for appropriate action by the U.S. Patent and Trademark Office are the following documents:

1. a response to the Office action dated May 8, 2002; and
2. a return postcard.

It is respectfully requested that the Patent and Trademark Office stamp the attached postcard with the filing date of these documents, and return it to our courier.

It is not believed that extensions of time or fees are required in conjunction with this submission. However, if extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned, and any fees are required therefor are hereby authorized to be charged to our Deposit Account Number 50-1824, referencing docket number 16517.031. Applicants likewise authorize a charge to Deposit Account Number 50-1824 for any fees related to the present submission that are not otherwise provided for in the accompanying documents.

Sincerely,



David R. Marsh (Reg. No. 41,408)
June E. Cohan (Reg. No. 43,741)

Enclosures

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re reissue application of:

David K. KOVALIC *et al.*

Appln. No. 09/684,016

Filed: October 10, 2000

For: Annotated Plant Genes

Group Art Unit: 1631

Examiner: S. Zhou

Attorney Docket: 16517.031 [38-21(15097)E]

Response to the Office Action Dated May 8, 2002

Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicants submit the following amendments and remarks for consideration.

Amendments**IN THE SPECIFICATION:**

Please replace the paragraphs beginning at page 1, line 29 and ending at page 3, line 10, with the following paragraphs:

Descriptions of biochemical and regulatory pathways are available from a number of well known academic and research organizations. An exemplary listing of such pathways can be found in US patent application Serial number 09/371,146, the entirety of which is herein incorporated herein by reference, see especially pages 1-312. Additionally, several web sites and databases contain information pertaining to biochemical pathways and regulatory pathways. Examples of such web sites include: cgsc.biology.yale.edu (the CGSC maintains a database of *E. coli* genetic information, including genotypes and reference information for the strains in the CGSC collection, gene names, properties, and linkage map, gene product information, and information on specific mutations); www.labmed.umn.edu (the University of Minnesota's

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Biocatalysis/Biodegradation web page provides a search engine for compounds, enzymes, microorganisms, chemical formulas CAS registry, EC accession and microbial biocatalytic reactions and biodegradation pathways primarily for xenobiotic chemical compounds such as methionine and threonine); wit.mcs.anl.gov/WIT2 (this website provides a functional overview which outlines metabolic pathways for organisms such as *E. coli*); ecocyc.PangeaSystems.com/ecocyc/ecocyc.html (this web site provides an overview of an *E. coli* metabolic map); www.biology.UCSD.edu (this web site provides information on signal transduction in higher plants); geo.nihs.go.jp (the Japanese National Institute of Health Science server provides information particularly on cell signaling networks); gifts.univ-mrs.fr (the Gene Intereactions in Fly Trans-world Server provides information on gene interactions, mostly centered on *Drosophila* gene interactions); sdb.bio.purdue.edu (this web site provides a data base of *Drosophila* genes); genome-www.stanford.edu (Stanford Genomic Research web site provides information on for example, *Sacchromyces* and *Arabidopsis*); www.psynix.co.uk (this web site provides illustrations and computer models of various cytokinins); www.sdsc.edu/Kinases/pk_home.html (this web site provides information on the protein kinase family of enzymes); transfac.gbf-braunschweig.de (the GBF web site provides information on regulatory genomic signals and regions, in particular those that govern transcriptional control); www.gcrdb.uthscsa.edu (this web site provides information on G-protein coupled receptors); www.biochem.purdue.edu (this web site provides information on secondary metabolism in *Arabidopsis*); home.wxs.nl/~pvsanten/mmp/mmp.html (this web site provides a flow chart of metabolic pathways); www.genome.ad.jp/kegg/regulation.html (this web site, the KEGG regulatory pathways web site, provides pathway maps, ortholog group tables, and molecular catalogs searchable data bases by enzyme, pathway, or EC number);

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capsulapedia.uchicago.edu/Capsulapedia/Metabolism/RegExpMet.shtml (this web site provides expression information);

www.zmbh.uniheidelberg.de/M_pneumoniae/genome/META/ALL_META.GIF (this web site provides a graphic of metabolic pathways and the ways these pathways interact);

moulon.inra.fr/cgi-bin/nph-acedb3.1/acedb/metabolisme (this web site provides information on *C. elegans* metabolic enzymes); www.gwu.edu/~mpb (this web site provides information on

metabolic pathways); www.bic.nus.edu.sg/pathwaydb.html (this web site provides links to biological pathways, such as metabolic pathways, developmental pathways, signal-transduction pathways, and genetic regulatory circuits); and www.scri.sari.ac.uk/bpp/charttxt.htm (this web site provides graphics of the metabolic pathways of diseased potato).

Please replace the paragraph at page 19, lines 3-10, with the following paragraph:

A PCR probe is a nucleic acid molecule capable of initiating a polymerase activity while in a double-stranded structure with another nucleic acid. Various methods for determining the structure of PCR probes and PCR techniques exist in the art. Computer generated searches using programs such as Primer3 (www-genome.wi.mit.edu/cgi-bin/primer/primer3.cgi), STSPipeline (www-genome.wi.mit.edu/cgi-bin/www-STSPipeline), or GeneUp (Pesole *et al.*, *BioTechniques* 25:112-123 (1998)), for example, can be used to identify potential PCR primers.

Please replace the paragraph at page 47 lines 5-13 with the following paragraph:

A microarray-based method for high-throughput monitoring of gene expression may be utilized to measure expression response Schena *et al.*, *Science* 270:467-470 (1995); on the world wide web at cmgm.stanford.edu/pbrown/array.html; Shalon, Ph.D. Thesis, Stanford University (1996). This approach is based on using arrays of DNA targets (e.g. cDNA inserts, colonies, or polymerase chain reaction products) for hybridization to a "complex probe" prepared with RNA

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extracted from a given cell line or tissue. The probe may be produced by reverse transcription of mRNA or total RNA and labeled with radioactive or fluorescent labeling. The probe is complex in that it contains many different sequences in various amounts, corresponding to the numbers of copies of the original mRNA species extracted from the sample.

In the claims:

Please amend the following claims:

11. (Once Amended) A substantially purified nucleic acid molecule comprising a fragment nucleic acid molecule having from about 30 to about 50 nucleotide residues of a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 48411.
12. (Once Amended) A substantially purified nucleic acid molecule comprising a fragment nucleic acid molecule having from about 50 to about 100 nucleotide residues of a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 48411.
13. (Once Amended) A substantially purified nucleic acid molecule comprising a fragment nucleic acid molecule having from about 30 to about 50 nucleotide residues; wherein said fragment nucleic acid molecule exhibits complete complementarity to a fragment of a second nucleic acid molecule having a nucleic acid sequence having the nucleotide sequence of SEQ ID NO: 48411 and a complete complement thereof.
14. (Once Amended) A substantially purified nucleic acid molecule having between 90% and 100% sequence identity with base pairs 1 through 123 of SEQ ID NO: 48411 and a complete complement thereof.

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Please insert the following new claim:

16. (New) A substantially purified nucleic acid molecule according to claim 15, wherein said nucleic acid molecule has the nucleic acid sequence of SEQ ID NO: 48411 or the complete complement thereof.

Remarks

In response to the finality of the restriction requirement Applicants have amended claims 11-15 to correspond in scope with the restriction. New claim 16 has been added, and following entry of this amendment, claims 11-16 will be pending. The amendments are supported throughout the original disclosure, for example at page 9-10 and in the sequence listing as originally filed. No new matter is added by the amendments.

I. Specification

Applicants have amended the specification to remove browser executable code in compliance with MPEP 608.01(b). In view of the foregoing, Applicants respectfully request withdrawal of the objection of record.

II. 35 U.S.C. §§ 101 utility and 112-1" paragraph

Claims 11-15 are rejected under 35 U.S.C. § 101 as allegedly not being supported by a specific and/or substantial utility, or a well-established utility.

Claims 11-15 stand rejected under 35 U.S.C. § 101 for allegedly not being supported by either specific and/or substantial utility, or a well-established utility. In addition, the Examiner asserts that the specification states that the specification while summarizing "pretty much modern biotechnology in general [but] never connects any of the specifically elected sequences to any particular specific utility," and that the "wishlist-like desire for utility of the claimed sequences seems to fall short of a readily available application." Office Action of May 8, at

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pages 4-5. The Office Action of May 8 continues on page 5 to assert that the utilities claimed for the nucleic acid are "neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds."

Applicants respectfully disagree. It is well-established that "when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983). The present specification describes many objectives that are met by the present invention. For example, the section "Nucleic Acid Markers and Probes," beginning on page 16 of the disclosure, sets forth the use of the claimed molecules as markers for indicating the presence of polymorphisms. Later, starting on page 42 at line 14, the specification discloses that markers can be used to prepare linkage maps, which are useful in plant breeding as they are an efficient means of determining the likelihood that traits will segregate. On page 17, starting at line 12, the specification discloses the use of the molecules as a markers for a biochemical processes or activities.

An Examiner must accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992). "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 U.S.P.Q.2d 1895, 1900 (Fed. Cir. 1996). As such, an Examiner "must do more than question operability – [the examiner] must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (CCPA 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); MPEP § 706.03(a)(1). No such

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factual reasons have been provided. Thus, the utilities disclosed by Applicants must be accepted as factually sound unless and until the Patent Office provides factual reasons that undermine the credibility of the assertion. Therefore, the Office has not met the requisite burden to impose a 35 U.S.C. § 101 rejection.

In sum, Applicants have asserted substantial, specific utilities for the claimed nucleic acid molecules of the invention, and absent specific evidence to the contrary, this assertion must be accepted. As such, Applicants have met their burden in establishing specific, "real-world" utilities for the claimed invention. In view of the above, Applicants contend that the claimed nucleic acid molecules are supported by specific and well-established utilities as disclosed in the specification. As such, withdrawal of this rejection is respectfully requested.

Claims 11-15 are rejected under 35 U.S.C. § 112 first paragraph as allegedly not being supported by a patentable use.

Applicants respectfully disagree with the Examiner's allegation that Claims 11-15 are not supported by a patentable use for the reasons set forth in the corresponding rejection under 35 U.S.C. 101. Applicants contend that the claimed invention is supported by a patentable utility and as such request respectfully request withdrawal of this rejection.

III. 35 U.S.C. § 112 first paragraph

Claims 11-15 are rejected under 35 U.S.C. § 112, 1st Paragraph, Written Description

Claims 11-15 stand rejected under 35 U.S.C. §112, 1st paragraph, as allegedly containing subject matter which was not described in the specification in a manner that reasonably conveys to one of ordinary skill in the art that the inventors had possession of the claimed invention at the time of filing. Applicants thank the Examiner for indicating that the skilled artisan could envision the detailed chemical structure of a nucleotide having the sequence of sequence of SEQ

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ID No. 48,411, and thus that Applicants had possession and met the written description requirement of 35 U.S.C. § 112 1st paragraph for this sequence. Office Action dated May 8, 2002.

Applicants respectfully traverse the rejection of claims 11-15 under 112 first paragraph. The purpose of the written description requirement is simply to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *See Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). In accordance with this purpose, Applicants need not "describe," in the sense of Section 112, all things that are encompassed by the claims. To contend otherwise would contradict established jurisprudence, which teaches that a patent may be infringed by technology developed after a patent issues. *United States Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1251, 9 U.S.P.Q.2d 1461, 1464 (Fed. Cir. 1989).

A related and equally well-established principle of patent law is that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-Mar-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985) (*quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (CCPA. 1981)). Thus, simply because the claimed nucleic acid sequences may also include other sequences does not require that Applicants describe each and every one of these molecules. Further, "a description as filed is presumed to be adequate, unless and until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption." *Federal Register* 66(4):1107,

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Written Description Guidelines (2001). In this regard, the Examiner is required to disclose "express findings of fact which support the lack of written description conclusion." *Id.*

Applicants have provided detailed chemical structures of the claimed nucleic acid sequences. These sequences provide "structural feature[s] possessed by members of the [claimed] genus that distinguish[es] them from others." *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). In contrast to the mere name "cDNA" provided in *Eli Lilly*, Applicants have provided detailed chemical structures. For at least this reason, it is respectfully submitted that the present claims meet the written description provision under 35 U.S.C. § 112, 1st paragraph.

The use of open claiming language (comprising) does not alter the fact that a skilled artisan would readily envision adequate written description support. The fact that nucleic acid sequences may be added to either end of the recited sequence is beside the point. Applicants have therefore reasonably conveyed to one skilled in the art possession of the claimed invention, even when additional sequences are added to either end. Indeed, as set forth in the original disclosure, the additional of extra nucleotides encoding, for example, bacterial ORI sequence or promoters are readily envisioned by those of ordinary skill upon reading the present specification.

For at least the foregoing reasons, the rejection under 35 U.S.C. § 112, 1st paragraph, written description, is traversed, and withdrawal of this rejection is respectfully requested.

IV. 35 U.S.C. § 112 second paragraph

Claims 13-14 are rejected under 35 U.S.C. § 112 second paragraph

The Examiner has rejected claims 13 and 14 as being vague and indefinite for the recitation of "complements thereof." The Examiner asserts that it is not clear what is meant by

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complements "complement," and that it could be complete complementarity or any percentage of complementarity.

Applicants respectfully disagree. Claims 13 recites a fragment nucleic acid molecule which exhibits "complete complementarity," and not simply "complementarity," to a second nucleic acid molecule. The specification at page 9, line 27 to page 10, line 4, addresses the meaning of "complete complementarity" such that one skilled in the art would be appraised of that which is claimed. Applicants respectfully submit that claims are not read in a vacuum and are to be interpreted in light of the specification. *In re Okuzawa*, 537 F.2d 545, 548, 190 U.S.P.Q. 464, 466 (CCPA 1976). Moreover, in addressing the requirement of 35 U.S.C. 112 second paragraph the Court of Appeals for the Federal Circuit stated if "claims, read in the light of the specifications, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no more." *Shatterproof Glass v. Libbey Owens Ford, Co.*, 758 F.2d 613, 225 U.S.P.Q. 634 (Fed. Cir. 1985) (quoting *Georgia-Pacific Corp. v. United States Plywood Corp.*, 258 F.2d 124, 136, 118 U.S.P.Q. 122, 132 (2d Cir.)).

In addition to the foregoing, Applicants submit the rejection of claim 14 is improper because one skilled in the art would be appraised of the metes and bounds of the subject matter claimed, as discussed above. However, in order to advance prosecution applicants have amended claim 14. Applicants submit they have met their burden under 35 U.S.C. §112 2nd paragraph and respectfully request the rejection to be withdrawn.

V. 35 U.S.C. § 102

Claims 13 and 14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Mahairas et al. (GenEmbl Acc. No. AQ451805, 4/21/1999).

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Claims 13 and 14 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Mahairas *et al.* Applicants respectively disagree. For a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference. *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 677, 7 U.S.P.Q.2d 1315, 1317 (Fed. Cir. 1988); *see also, Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986) (discussing the requirement of a reference employed in an anticipation rejection under § 102 "to meet every element of the claimed invention").

With regard to claim 13, Applicants submit that whatever else the Mahairas reference teaches, it does not teach a nucleic acid having from about 30 to about 50 nucleotide residues, where the fragment nucleic acid molecule exhibits complete complementarity to a fragment of the elected nucleic acid molecule (SEQ ID NO: 48411). Moreover, Applicants respectfully direct the Examiner's attention to the definition of complete complementarity at page 10, lines 2-4 of the disclosure. Moreover, with regard to claim 14, whatever else the Mahairas reference teaches it does not teach a substantially purified nucleic acid molecule having between 90% and 100% sequence identity with base pairs 1 through 123 of SEQ ID NO: 48411. Because the Mahairas reference does not teach every limitation of the claim, Applicant's respectfully submit that the rejection is improper and therefore request that the rejection be withdrawn.

Conclusion

In view of the above, each of the presently pending claims in the application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested in withdraw the outstanding rejections of the claims and to pass this application to issues. The Examiner is invited to contact the undersigned at (202) 942-5068 with respect to any unresolved issues remaining in this application.

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The Examiner is encouraged to contact the undersigned should any additional information be necessary for allowance.

Respectfully submitted,



David R. Marsh (Reg. No. 41,408)

June E. Cohan (Reg. No. 43,741)

Date: August 8, 2002

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MARKED-UP VERSION OF AMENDMENTS PURSUANT TO 37 C.F.R. 121

IN THE SPECIFICATION:

Please replace the paragraphs beginning at page 1, line 29 and ending at page 3, line 10, with the following paragraphs:

Descriptions of biochemical and regulatory pathways are available from a number of well known academic and research organizations. An exemplary listing of such pathways can be found in US patent application Serial number 09/371,146, the entirety of which is herein incorporated herein by reference, see especially pages 1-312. Additionally, several web sites and databases contain information pertaining to biochemical pathways and regulatory pathways.

Examples of such web sites or data bases include: [<http://cgsc.biology.yale.edu>]

cgsc.biology.yale.edu (the CGSC maintains a database of *E. coli* genetic information, including genotypes and reference information for the strains in the CGSC collection, gene names, properties, and linkage map, gene product information, and information on specific mutations);

[<http://www.labmed.umn.edu>] www.labmed.umn.edu (the University of Minnesota's

Biocatalysis/Biodegradation web page provides a search engine for compounds, enzymes, microorganisms, chemical formulas CAS registry, EC accession and microbial biocatalytic reactions and biodegradation pathways primarily for xenobiotic[,] chemical compounds such as methionine[,] and threonine); [<http://wit.mcs.anl.gov/WIT2>] wit.mcs.anl.gov/WIT2 (this website provides a functional overview which outlines metabolic pathways for organisms such as *E. coli*); [<http://ecocyc.PangeaSystems.com/ecocyc/ecocyc.html>]

ecocyc.PangeaSystems.com/ecocyc/ecocyc.html (this web site provides an overview of an *E. coli* metabolic map); [<http://www.biology.UCSD.edu>] www.biology.UCSD.edu (this web site provides information on signal transduction in higher plants); [<http://geo.nihs.go.jp>]

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geo.nih.go.jp (the Japanese National Institute of Health Science server provides information particularly on cell signaling networks); [<http://gifts.univ-mrs.fr>] gifts.univ-mrs.fr (the Gene Interactions in Fly Trans-world Server provides information on gene interactions, mostly centered on *Drosophila* gene interactions); [<http://sdb.bio.purdue.edu>] sdb.bio.purdue.edu (this web site provides a data base of *Drosophila* genes); [<http://genome-www.stanford.edu>] genome-www.stanford.edu (Stanford Genomic Research web site provides information on for example, *Sacchromyces* and *Arabidopsis*); [<http://www.psynix.co.uk>] www.psynix.co.uk (this web site provides illustrations and computer models of various cytokinins); [http://www.sdsc.edu/Kinases/pk_home.html] www.sdsc.edu/Kinases/pk_home.html (this web site provides information on the protein kinase family of enzymes); [<http://transfac.gbf-braunschweig.de>] transfac.gbf-braunschweig.de (the GBF web site provides information on regulatory genomic signals and regions, in particular those that govern transcriptional control); [<http://www.gcrdb.uthscsa.edu>] www.gcrdb.uthscsa.edu (this web site provides information on G-protein coupled receptors); [<http://www.biochem.purdue.edu>] www.biochem.purdue.edu (this web site provides information on secondary metabolism in *Arabidopsis*); [<http://home.wxs.nl/~pvsanten/mmp/mmp.html>] home.wxs.nl/~pvsanten/mmp/mmp.html (this web site provides a flow chart of metabolic pathways); [<http://www.genome.ad.jp/kegg/regulation.html>] www.genome.ad.jp/kegg/regulation.html (this web site, the KEGG regulatory pathways web site, provides pathway maps, ortholog group tables, and molecular catalogs searchable data bases by enzyme, pathway, or EC number); [<http://capsulapedia.uchicago.edu/Capsulapedia/Metabolism/RegExpMet.shtml>] capsulapedia.uchicago.edu/Capsulapedia/Metabolism/RegExpMet.shtml (this web site provides expression information); [<http://www.zmbh.uni->

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heidelberg.de/M_pneumoniae/genome/META/ALL_META.GIF] www.zmbh.uni-heidelberg.de/M_pneumoniae/genome/META/ALL_META.GIF (this web site provides a graphic of metabolic pathways and the ways these pathways interact); [http://moulon.inra.fr/cgi-bin/nph-acedb3.1/acedb/metabolisme] moulon.inra.fr/cgi-bin/nph-acedb3.1/acedb/metabolisme (this web site provides information on *C. elegans* metabolic enzymes); [http://www.gwu.edu/~mpb] www.gwu.edu/~mpb (this web site provides information on metabolic pathways); [http://www.bic.nus.edu.sg/pathwaydb.html] www.bic.nus.edu.sg/pathwaydb.html (this web site provides links to biological pathways, such as metabolic pathways, developmental pathways, signal-transduction pathways, and genetic regulatory circuits); and [http://www.scri.sari.ac.uk/bpp/charttxt.htm] www.scri.sari.ac.uk/bpp/charttxt.htm (this web site provides graphics of the metabolic pathways of diseased potato).

Please replace the paragraph at page 19, lines 3-10, with the following paragraph:

A PCR probe is a nucleic acid molecule capable of initiating a polymerase activity while in a double-stranded structure [to] with another nucleic acid. Various methods for determining the structure of PCR probes and PCR techniques exist in the art. Computer generated searches using programs such as Primer3 [(www-genome.wi.mit.edu/cgi-bin/primer/primer3.cgi)] [www-genome.wi.mit.edu/cgi-bin/primer/primer3.cgi], STSPipeline [(www-genome.wi.mit.edu/cgi-bin/www-STS_Pipeline)] [www-genome.wi.mit.edu/cgi-bin/www-STS_Pipeline], or GeneUp (Pesole *et al.*, *BioTechniques* 25:112-123 (1998)), for example, can be used to identify potential PCR primers.

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Please replace the paragraph at page 47 lines 5-13 with the following paragraph:

A microarray-based method for high-throughput monitoring of gene expression may be utilized to measure expression response Schena *et al.*, *Science* 270:467-470 (1995); [<http://cmgm.stanford.edu/pbrown/array.html>] on the world wide web at cmgm.stanford.edu/pbrown/array.html; Shalon, Ph.D. Thesis, Stanford University (1996). This approach is based on using arrays of DNA targets (e.g. cDNA inserts, colonies, or polymerase chain reaction products) for hybridization to a "complex probe" prepared with RNA extracted from a given cell line or tissue. The probe may be produced by reverse transcription of mRNA or total RNA and labeled with radioactive or fluorescent labeling. The probe is complex in that it contains many different sequences in various amounts, corresponding to the numbers of copies of the original mRNA species extracted from the sample.

IN THE CLAIMS:

11. (Once Amended) A substantially purified nucleic acid molecule comprising a fragment nucleic acid molecule having from about 30 to about 50 nucleotide residues of a nucleic acid molecule [selected from the group consisting] having the nucleotide sequence of SEQ ID NO: 48411[1 through SEQ ID NO: 463,173].
12. (Once Amended) A substantially purified nucleic acid molecule comprising a fragment nucleic acid molecule having from about 50 to about 100 nucleotide residues of a nucleic acid molecule [selected from the group consisting] having the nucleotide sequence of SEQ ID NO: 48411[1 through SEQ ID NO: 463,173].

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13. (Once Amended) A substantially purified nucleic acid molecule comprising a fragment nucleic acid molecule having from about 30 to about 50 nucleotide residues; wherein said fragment nucleic acid molecule exhibits complete complementarity to a fragment of a second nucleic acid molecule having a nucleic acid sequence [selected from the group consisting] having the nucleotide sequence of SEQ ID NO: 48411 [1 through SEQ ID NO: 463,173] and a complete complement [complements] thereof.

14. (Once Amended) A substantially purified nucleic acid molecule having between 90% and 100% sequence identity with base pairs 1 through 123 [a second nucleic acid molecule selected from the group consisting] of SEQ ID NO: 48411 [1 through SEQ ID NO: 463,173] and a complete complement [complements] thereof.

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Atty. Docket No.: 16517.031	7788	We are transmitting 23 page(s) (including this cover sheet)	
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MESSAGE			
Per my telephone conversation with Bill Phillips on April 9, 2003, please match the attached documents with the file for U.S. Appln. No. 09/684,016.			
Thank you.			

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Atty Docket No: 16517.031
Date: November 8, 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): KOVALIC *et al.*
Appln. No.: 09/684,016
Filing Date: October 10, 2000
Title: Annotated Plant Genes

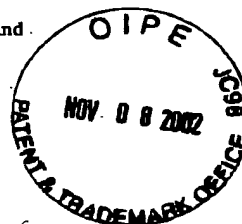
Art Unit: 1631
Examiner: S. Zhou

Commissioner for Patents
Washington, DC 20231

Sir:

Please place the U.S. Patent & Trademark Office receipt stamp hereon to acknowledge receipt of the following:

1. a Transmittal Letter (in duplicate);
2. a Response to Notice of Non-Responsive Communication;
3. a photocopy of the Response to the Office Action Dated May 8, 2002; and
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Danielle M. Edwards (1195A)

ARNOLD & PORTER

202.942.5000
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November 8, 2002

Commissioner for Patents
Washington, DC 20231

Re: U.S. Application No. 09/684,016
Filed: October 10, 2000
Title: Annotated Plant Genes
Applicants: KOVALIC *et al.*
Atty. Docket: 16517.031

Sir:

The following documents are forwarded herewith for appropriate action by the U.S. Patent and Trademark Office (PTO):

1. a Response to Notice of Non-Responsive Communication;
2. a photocopy of the Response to the Office Action Dated May 8, 2002; and
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Please stamp the attached postcard with the filing date of these documents and return it to our courier.

In the event that extensions of time beyond those petitioned for herewith are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Applicants do not believe any fees are due in conjunction with this filing. However, if any fees under 37 C.F.R. §§ 1.16 or 1.17 are required in the present application, including any fees for extensions of time, then the Commissioner is hereby authorized to charge such fees to Arnold & Porter Deposit Account No. 50-2387 referencing matter number 16517.031. A duplicate copy of this letter is enclosed.

Respectfully submitted,



David R. Marsh (Reg. No. 41,408)

June E. Cohan (Reg. No. 43,741)

Danielle M. Edwards, Law Clerk (Reg. No. 51,645)

Enclosures